Remarks

Claims 1-29 are pending in the subject application. Applicants acknowledge that restriction has been withdrawn. Claim 26 is amended above to correct a typographical omission that was noticed by the Examiner. No new matter is added by this amendment. Favorable consideration of the claims in view of the following remarks is respectfully requested.

Claims 1-29 are rejected under 35 USC §112, first paragraph, as nonenabled by the subject specification. Applicants respectfully traverse. The comments set forth in support of this rejection at Office Action page 3, first two paragraphs, can be summarized as asserting that the specification fails to teach anything that was not specifically exemplified. This is not in accord with how one of ordinary skill in the art would interpret teachings of the specification, nor is it in accord with the law. An application may be entirely prophetic so long as its teachings are true and are specific enough for one of skill in the art to follow those teachings and practice the invention. That is all that is required, nothing more. See, *In re Marzocchi,* 169 USPQ 367 (CCPA 1971). The law requires only objective enablement which may be accomplished by illustrative examples, broad terminology, or a combination of both as in the subject application. In the responses of record in parent application 09/070,844 (the arguments and submissions of which are herein incorporated by reference) Applicants have explained exactly how the combination of specific examples, coupled with broad teachings, fully enables the claimed invention. Under such circumstances, the only relevant concern of the Patent Office is whether the teachings are true. See, *In re Marzocchi, supra,* at 369. Applicants' teachings have been proven to be true as made clear by the Second and Third Declarations of Philip Miller, Ph. D., of record in the parent application, and copies of which are attached hereto for the Examiner's convenience. As is thoroughly explained in the Third Miller Declaration, the pending claims are fully enabled, because one of skill in the art is taught the benefits of both increased nitrogen assimilation and decreased nitrogen assimilation. Although the specification exemplifies the invention using coding sequences obtained from *Chlorella,* it also explicitly teaches that a wide variety of GDH coding sequences were publicly available, widely known, and had been known for at least 10 years before the priority date of this application (See attached Communication dated December 19, 2001 from the parent application, showing the results of a March 1995 Genbank search.). Accordingly, it is undeniable that Applicants teach and were effectively in

possession of a wide variety of GDH encoding sequences at the time this application was first filed.

Next, the Examiner is correct that in some organisms NAD-GDH tends to be a nuclear-encoded mitochondria-associated enzyme (although microbial NAD-GDHs are not mitrochondria associated), whereas NADP-GDH tends to be chloroplast-associated; and that NADP-GDHs have been found to be associated with amination, while NAD-GDHs have been found to be associated with deamination. In this respect, the detailed examples provided by Applicants describing characteristics of the *Chorella* GDH isoenzymes (α and β subunits) are particularly useful. NAD-GDH enzymes, which tend to be deaminating (as is the β-subunit), would be readily recognized by the ordinary artisan in view of the subject teachings to be useful for decreasing nitrogen metabolism (and, because of the associated inverse effect on carbon metabolism, thereby increasing accumulation of carbohydrates in the transgenic plant). See, for example, page 4, lines 24-30 and page 10, lines 4-9 of the specification.

Regarding the assertion that use of fragments of GDH genes are not enabled, Applicants respectfully assert that it was routine in the art for ordinary artisans to predictably and accurately produce dozens and dozens of various fragments in one afternoon from any known gene using time-controlled *Bal*31 exonuclease digestion of a DNA of interest, and this would readily be followed by expression of the resulting fragments and routine screening of the expression products, as is taught at page 30, lines 12-20 of the specification. Examples teachings expression methods and routine screening for functional product are explicitly set forth in the specification. Accordingly, because use of *Bal*31 exonuclease had been routinely practiced by ordinary artisans for more than 10 years before the priority date of this application, and because Applicants have provided specific examples demonstrating how GDH DNAs of interest can be expressed and their activity verified, fragments of full length GDH genes for use in connection with the teachings herein are clearly enabled by the specification.

Finally, regarding the Office Action's assertion at page 4 that no use is described for plants having decreased nitrogen metabolism, Applicants respectfully point to page 4, lines 24-30, wherein the application teaches that alteration of nitrogen assimilation is inversely related to carbon metabolism (therefore as nitrogen assimilation decreases, carbohydrate accumulation increases), and teaching the β-homohexamer (and, similarly, deaminating GDHs, including NAD-GDHs) can be used to favor accumulation of carbohydrates in fruits and other storage

organs (page 10, lines 7-9 of the specification). See the Third Miller Declaration, paragraphs 2 and 3. Accordingly, Applicants respectfully assert that they have enabled the claimed invention and request reconsideration in view of the foregoing.

Next, Claims 1-29 are rejected 35 USC §112, first paragraph, as lacking sufficient written description for reasons set forth at page 5 of the Office Action. Applicants respectfully traverse. Contrary to what is asserted in the Office Action, Applicants' specification is not limited to describing only those nucleic acids specifically exemplified. Rather, as explained above, Applicants explicitly taught that a wide variety of GDH-encoding sequences were publicly available and could be used by those of ordinary skill in the art according to the teachings herein. Applicants have submitted the results of a March 1995 Genbank search proving the truth of these teachings. These sequences were undeniably in the public domain and were referred to as a group by explicit reference in the specification. Accordingly, to those skilled in the art it is abundantly clear that Applicants have provided enough information to make it clear they were in possession of the claimed genus at the time the application was filed. Reconsideration is respectfully requested.

Claims 22-29 are rejected under 35 USC §112, second paragraph, as indefinite. Regarding claim 22, Applicants respectfully assert that the term "cells" is very clear. It means "more than one cell." Regarding claims 23-29 and the phrase "transgenic cells according to claim 22", Applicants assert that claim 22 refers to "transgenic plant cells," thus antecedent basis for the recited phrase is adequate. It is clear to the ordinary artisan that the transgenic cells of claim 22 that are referred to in each of claims 23-29 are transgenic plant cells. Applicants have amended claim 26 above to provide clarification regarding the chloroplast transit peptide. Applicants thank the Examiner for her careful reading of the claims. Finally, claim 29 is rejected for the phrase "said tissue specific initiation region." Claim 29 refers to claim 28, which states, in part, "... wherein said transcription *initiation region is tissue specific*." Accordingly, the cited phrase finds explicit antecedent basis in the preceding claim. In view of the forgoing, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejections.

Next, Applicants respectfully traverse the §102 and 103 rejections set forth at pages 6-7 and 9 of the Office Action which are based on Long *et al.*. The cited reference Long *et al.* is not enabling. It fails to provide the ordinary artisan with any expectation of success. In fact, the cited reference provides nothing but an invitation to experiment. Although Long *et al.* states that

"Plant nitrogen metabolism has been altered by transformation with a highly active assimilatory bacterial glutamate dehydrogenase gene," no details whatsoever are provided. There is no teaching of how one would identify such a gene. No DNA sequence information is provided. No source plasmid is identified. No restriction enzyme cleavage information is provided. There is no teaching regarding source organism for the gene. No transformation vector is provided. No transformation methods are suggested. There is no teaching regarding the target plant species. In fact, there is no proof that any transgenic plant was obtained, nor even any transgenic plant cells. Although the authors assert that nitrogen metabolism in some type of purportedly transgenic plant was altered, they do not tell in what way it was altered. They speculate that "increasing the activity of plant nitrogen metabolism enzymes may alter plant growth", but maybe not. They further speculate that "increased yield and protein content . . . may result," but maybe not. They state that their unidentified bacterial GDS gene "has been altered by PCR . . . to modify coding region" yet they provide no guidance as to what alterations were made. They assert that the 5′ non-coding region of the unidentified GDS gene has been altered, but they don't tell how. They assert that the 3′ non-coding region has been altered, but they don't tell how. They state that "certain codons likely to inhibit expression . . . have been altered", but they don't tell how. Finally, they conclude "The effects of the various sequence substitutions [none of which are identified] on gene expression in plant cells [unidentified] compared to the unmodified gene [unidentified] will be reported." The ordinary artisan is clearly left to speculate whether any effects were observed or not. There is no teaching that the experiments in unidentified plant cells using unidentified transformation techniques (successful?) with an unidentified transformation vector, which may or may not have contained an unidentified bacterial GDH sequence, which was purportedly modified in a number of teasingly unspecified ways, had any observable effects at all.

It is irrefutable that to be a sufficiently anticipatory prior art reference under §102, the prior art reference must be enabling. The Court of Appeals for the Federal Circuit has stated, "when there is not disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all of the disclosure related to the process is within the skill of the art." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, at 1005 (Fed. Cir. 1997). Long *et al.* discloses none of their starting materials. Long *et al.*

discloses none of the conditions under which their processes were performed. In view of the foregoing, it is abundantly clear that this one paragraph abstract fails to meet the requirements of an anticipatory reference and the rejection should be withdrawn.

Further, regarding obviousness, Long *et al.*, provides nothing but the suggestion to experiment to one of ordinary skill in the art. It is woefully lacking in specifics of any kind, whether experimental procedures or resulting data, which might provide the ordinary artisan with the required reasonable expectation of success. To support an obviousness rejection, one must find both the suggestion, and the reasonable expectation of success, in the prior art. *In re Dow Chemical Co.*, 5 USPQ2d 1529,1531 (Fed. Cir. 1988). The reference is not enabling and fails to provide any expectation of success to the ordinary skilled artisan. Accordingly no *prima facie* case of obviousness has been set forth, and the rejection must be withdrawn. Reconsideration is respectfully requested.

Claims 1-5, 10, 13-22, 24, and 26-29 are rejected under 35 USC §102(e) as anticipated by Lightfoot *et al.* (US Patent 5,998,700). The '700 patent has a filing date of July 1996, which is after the October 1995 priority date of this application. Accordingly, the '700 patent is not available as a §102 reference. Reconsideration is respectfully requested.

Claims 1-5, 10, and 13-29 are rejected under 35 USC §102(e) as anticipated by Lightfoot *et al.* (US Patent 6,329,573). The '573 patent has a filing date of July 1996, which is after the October 1995 priority date of this application. Accordingly, the '573 patent is not available as a §102 reference. Reconsideration is respectfully requested.

Claims 1-4, 10, 13, and 17 are rejected under 35 USC §102(e) as anticipated by Good *et al.* (US Patent 6,084,153). The '153 patent has a filing date of February 1996, which is after the October 1995 priority date of this application. Accordingly, the '153 patent is not available as a §102 reference. Reconsideration is respectfully requested.

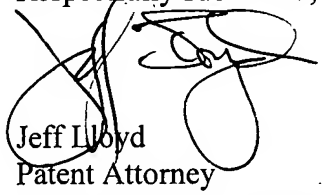
Upon indication that claims are otherwise allowable, Applicants will file a terminal disclaimer to address the double-patenting rejection.

In view of the foregoing remarks, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Petition and Fee for Extension of Time